

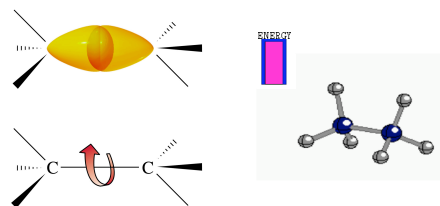
Chapter 2

An Introduction to Organic Compounds

Conformations

Adapted from Profs. Turro & Breslow, Columbia University and Prof. Irene Lee, Case Western Reserve University

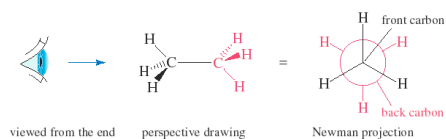
Conformations of Alkanes: Rotation about Carbon–Carbon Bonds



Conformational Analysis

Drawing Acyclic Molecules

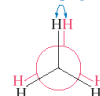
• Newman Projections



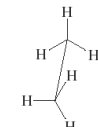
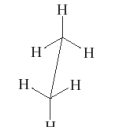
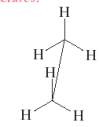
Conformational Analysis

Drawing Acyclic Molecules

Newman projections: $\theta = 0^\circ$



Sawhorse structures:

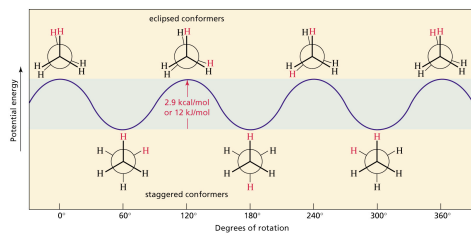


eclipsed, $\theta = 0^\circ$

staggered, $\theta = 60^\circ$

skew, $\theta = \text{anything else}$

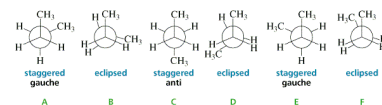
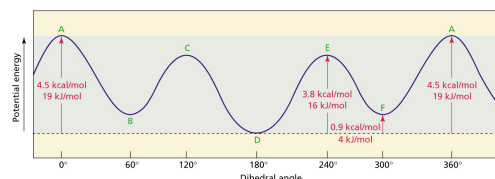
Different Conformations of Ethane



- A staggered conformer is more stable than an eclipsed conformer
- Torsional strain: repulsion between pairs of bonding electrons

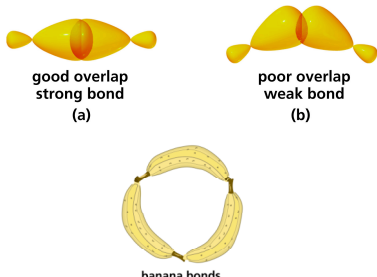
Conformations of *n*-Butane

- Steric strain: repulsion between the electron clouds of atoms or groups



Cycloalkanes: Ring Strain

- Angle strain results when bond angles deviate from the ideal 109.5° bond angle



The Shapes of Cycloalkanes: Planar or Nonplanar?

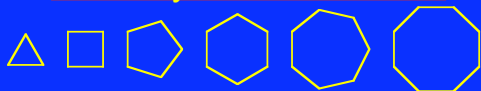
Adolf von Baeyer (19th century)

- Assumed cycloalkanes were planar polygons.
- Believed distortion of bond angles from 109.5° gives angle strain to some cycloalkanes.
- One for two is great in baseball.

Types of Strain

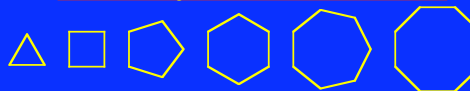
- Torsional strain**
strain that results from eclipsed bonds (measure of the dihedral angle)
- Van der Waals strain or (**Steric strain**)
strain that results from atoms being too close together.
- Angle strain** results from distortion of bond angles from normal values, for a tetrahedron 109.5°

Measuring Strain in Cycloalkanes



- Heats of combustion can be used to compare stabilities of isomers.
- But cyclopropane, cyclobutane, etc. are not isomers.
- All heats of combustion increase as the number of carbon atoms increase.

Measuring Strain in Cycloalkanes



- Therefore, divide heats of combustion by number of carbons and compare heats of combustion on a "per CH_2 group" basis.

Heats of Combustion in Cycloalkanes

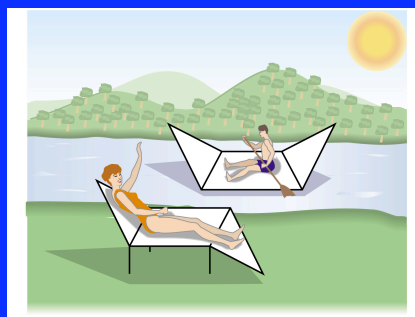
Cycloalkane	kJ/mol	Per CH ₂
Cyclopropane	2,091	697
Cyclobutane	2,721	681
Cyclopentane	3,291	658
Cyclohexane	3,920	653
Cycloheptane	4,599	657
Cyclooctane	5,267	658
Cyclononane	5,933	659
Cyclodecane	6,587	659

Heats of Combustion in Cycloalkanes

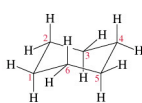
- Cycloalkane kJ/mol Per CH₂
- According to Baeyer, cyclopentane should have less angle strain than cyclohexane.
- Cyclopentane 3,291 658
- Cyclohexane 3,920 653
- The heat of combustion per CH₂ group is less for cyclohexane than for cyclopentane.
- Therefore, cyclohexane has less strain than cyclopentane.

Conformations of Cyclohexane

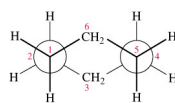
- Heat of combustion suggests that angle strain is unimportant in cyclohexane.
- Tetrahedral bond angles require nonplanar geometries.
- The chair and boat conformations.



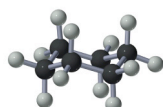
- The chair conformation of cyclohexane is free of strain



chair conformer of cyclohexane

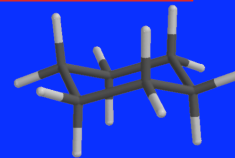
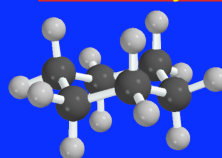


Newman projection of the chair conformer



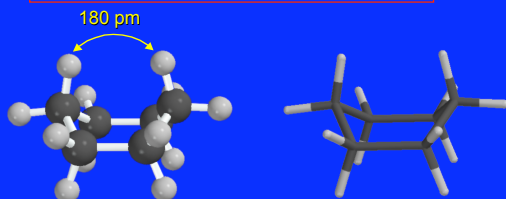
ball-and-stick model of the chair conformer of cyclohexane

Chair is the most stable conformation of cyclohexane



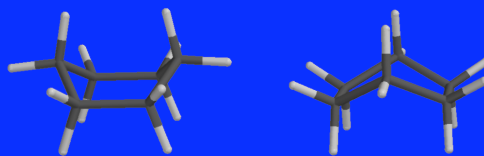
- All of the bonds are staggered and the bond angles at carbon are close to tetrahedral.

Boat conformation is less stable than the chair



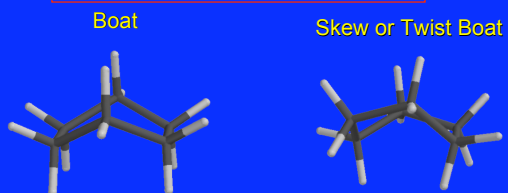
- All of the bond angles are close to tetrahedral but close contact between flagpole hydrogens causes strain in boat.

Boat conformation is less stable than the chair



- Eclipsed bonds gives torsional strain to boat.

Skew boat is slightly more stable than boat



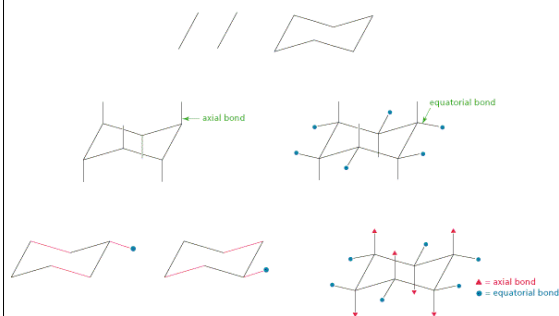
- Less van der Waals strain and less torsional strain in skew boat.

Generalization

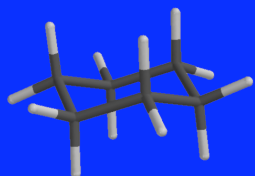
- The chair conformation of cyclohexane is the most stable conformation and derivatives of cyclohexane almost always exist in the chair conformation

Axial and Equatorial Bonds in Cyclohexane

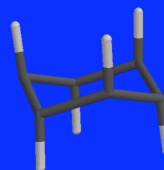
Drawing Cyclohexane



The 12 bonds to the ring can be divided into two sets of 6.

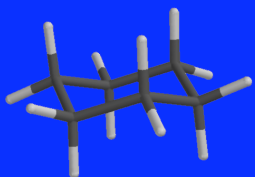


6 Bonds are axial

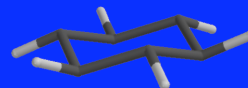


Axial bonds point "north and south"

The 12 bonds to the ring can be divided into two sets of 6.



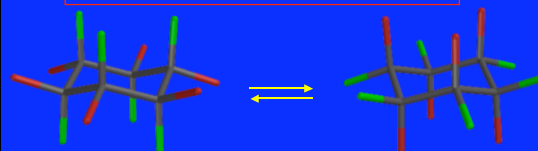
6 Bonds are equatorial



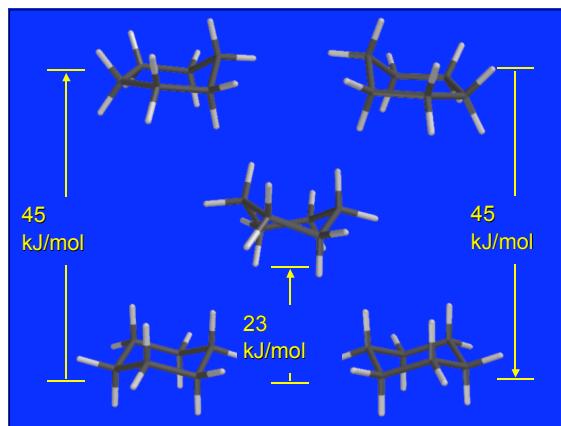
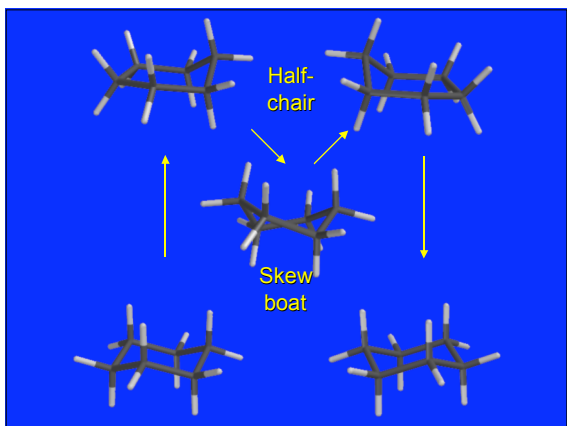
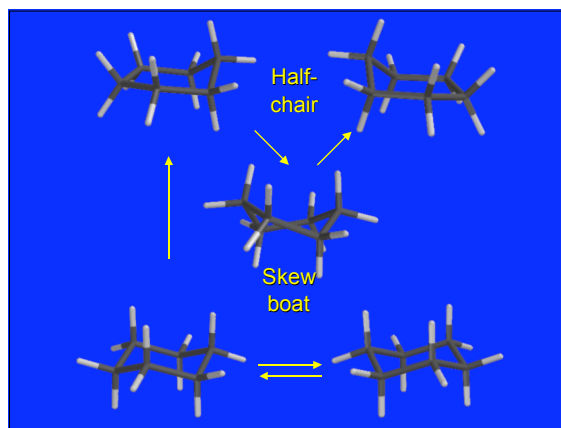
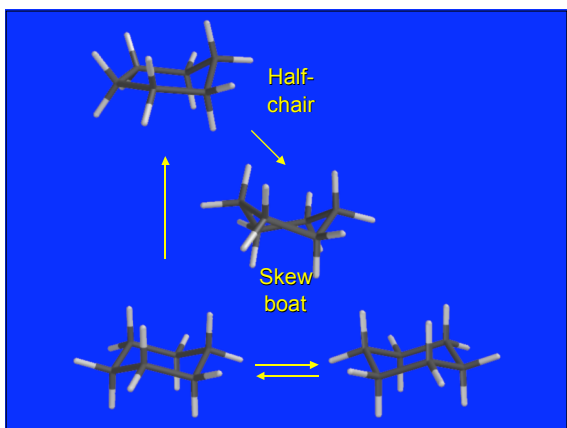
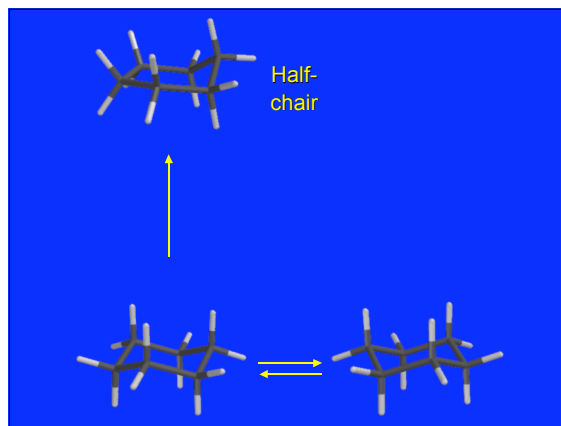
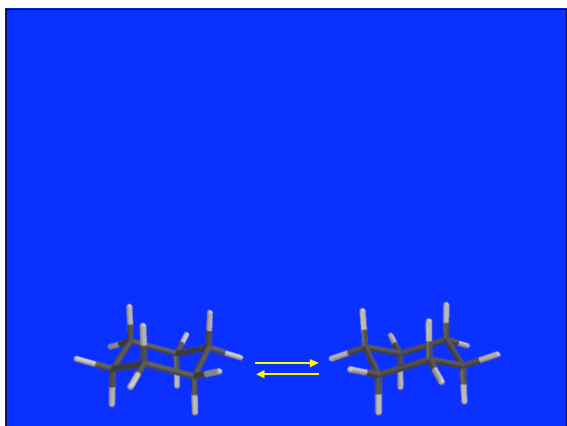
Equatorial bonds lie along the equator

*Conformational
Inversion
(Ring-Flipping) in
Cyclohexane*

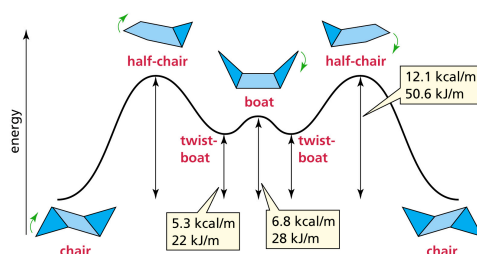
Conformational
Inversion



- chair-chair interconversion (ring-flipping)
- rapid process (activation energy = 45 kJ/mol)
- all axial bonds become equatorial and vice versa



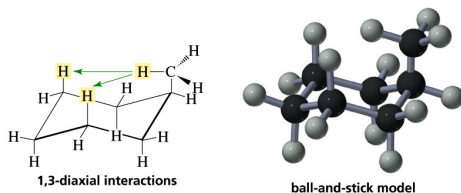
The Conformations of Cyclohexane and Their Energies



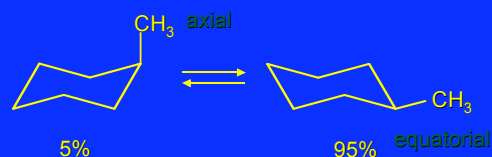
Conformational Analysis of Monosubstituted Cyclohexanes

- most stable conformation is chair
- substituent is more stable when equatorial

Steric Strain of 1,3-Diaxial Interaction in Methylcyclohexane

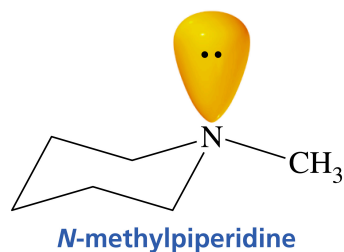


Methylcyclohexane

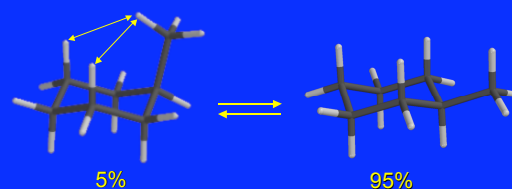


- Chair chair interconversion occurs, but at any instant 95% of the molecules have their methyl group equatorial.
- An axial methyl group is more crowded than an equatorial one.

- Is this the most stable conformer?

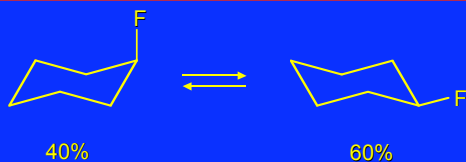


Methylcyclohexane



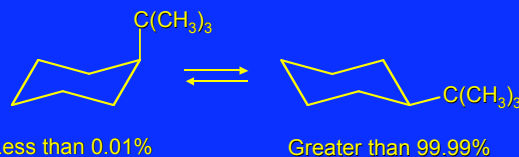
- Hydrogen atoms closer than 2.4 Angstroms will cause steric strain.
- This is called a "1,3-diaxial repulsion" a type of van der Waals strain or Steric strain.

Fluorocyclohexane



- Crowding is less pronounced with a "small" substituent such as fluorine.
- Size of substituent is related to its branching.

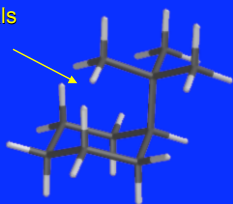
tert-Butylcyclohexane



- Crowding is more pronounced with a "bulky" substituent such as *tert*-butyl.
- *tert*-Butyl is highly branched.

tert-Butylcyclohexane

van der Waals strain due to 1,3-diaxial repulsions



- The larger the substituent on a cyclohexane ring, the more the equatorial substituted conformer will be favored

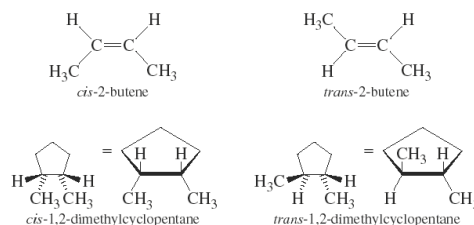
Table 2.10 Equilibrium Constants for Several Monosubstituted Cyclohexanes at 25 °C

Substituent	Axial	K_{eq}	Equatorial	Substituent	Axial	K_{eq}	Equatorial
H		1		CN		1.4	
CH ₃		18		F		1.5	
CH ₂ CH ₂		21		Cl		2.4	
CH ₃ CH		35		Br		2.2	
CH ₃ CH		4800		I		2.2	
CH ₃ C(CH ₃) ₂				HO		5.4	

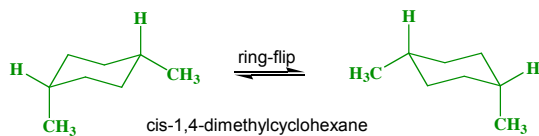
$$K_{eq} = [\text{equatorial conformer}]/[\text{axial conformer}]$$

Disubstituted Cyclohexanes Cis-trans Isomerism

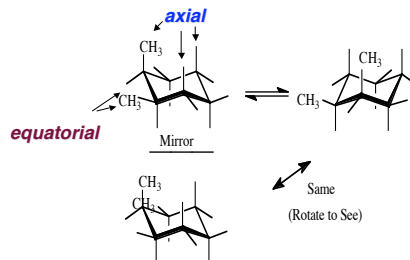
Cyclic Alkanes Stereochemistry Cis-Trans Isomers



The Chair Conformers of *cis*-1,4-Dimethylcyclohexane

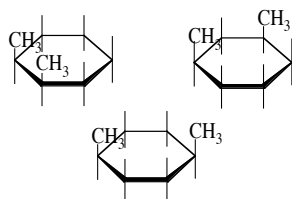


1,2-disubstituted-*cis*-cyclohexane Stereochemistry



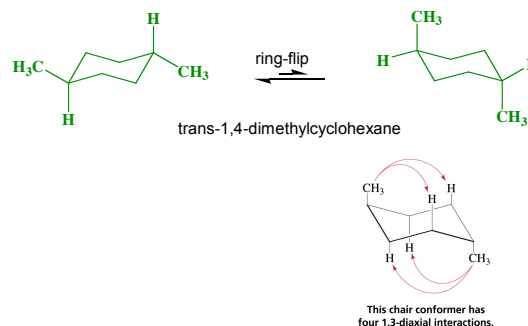
Cyclohexane Stereochemistry

Drawings: Cis isomers & the need for perspective



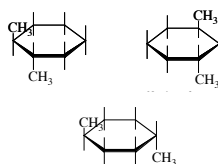
Are the methyl groups axial or equatorial?
What is the actual conformational shape of the cyclohexane ring?

The Chair Conformers of *trans*-1,4-Dimethylcyclohexane

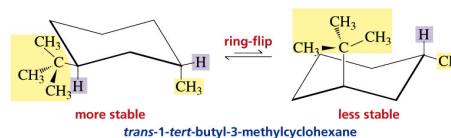


Cyclohexane Stereochemistry

Trans isomers



1-*tert*-Butyl-3-Methylcyclohexane

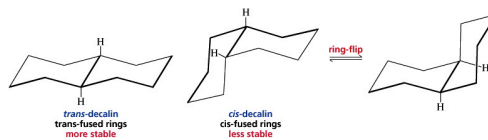


Cyclohexane Stereochemistry Cis-Trans Isomers

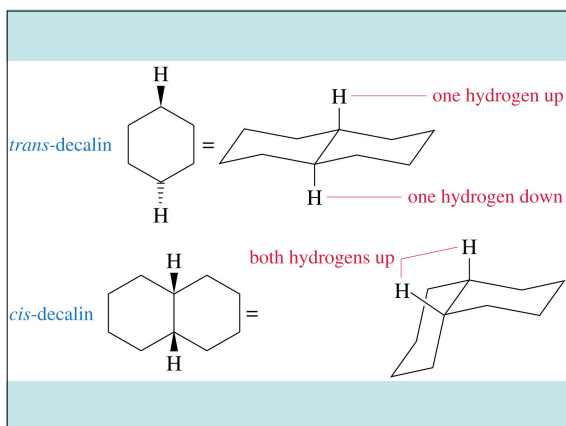
Position	cis	trans
1,2	e,a or a,e	e,e or a,a
1,3	e,e or a,a	a,e or e,a
1,4	e,a or a,e	e,e or a,a

Complete the Table: a = axial; e = equatorial

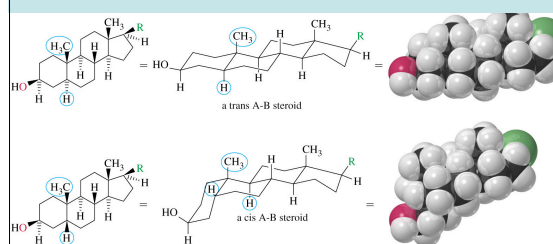
Conformations of Fused Rings



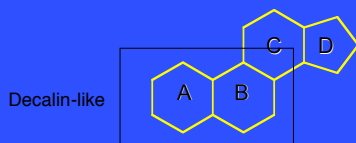
- Trans-fused cyclohexane ring is more stable than cis-fused cyclohexane ring



Steroids



Structure of Steroids



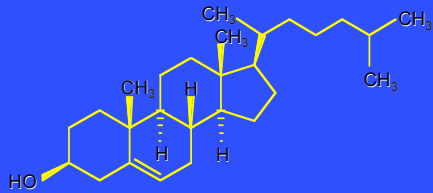
- Fundamental framework of steroids is a tetracyclic carbon framework.
- Cholesterol is an important steroid found in all plants and animals.

Structure of Cholesterol



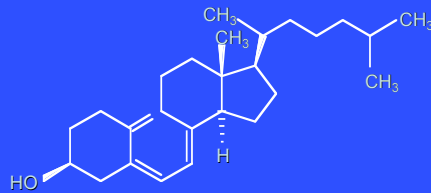
- What principal function is present?
- Is the A/B ring system cis or trans?

Cholesterol



- Cholesterol is essential to life. It is the biosynthetic precursor to a large number of important molecules: **Vitamin D**, **Bile acids**, **Corticosteroids**, **Sex hormones**.

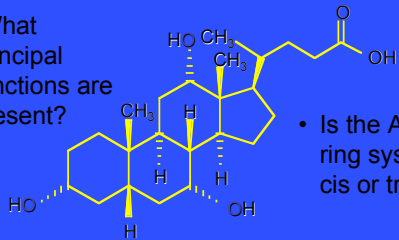
Vitamin D₃



- Insufficient sunlight can lead to a deficiency of vitamin D₃, interfering with Ca²⁺ transport and bone development. Rickets may result; as well as very bad moods.

Cholic Acid

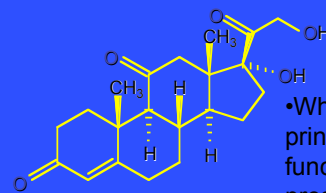
•What principal functions are present?



- Is the A/B ring system cis or trans?

•Oxidation in the liver degrades cholesterol to produce Cholic acid which is the most abundant of the bile acids.

Cortisone

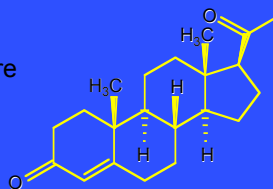


•What principal functions are present?

•Corticosteroids are involved in maintaining electrolyte levels, in the metabolism of carbohydrates, and in mediating allergic reactions by suppressing the immune system..

Progesterone

•What principal functions are present?



- Supresses ovulation during pregnancy.